

**Wellcome PhD Supervisors
Mental and Cognitive Health Theme**

David M Clark

Social Anxiety Disorder: Cognitive Processes and Treatment

Abstract: Social anxiety disorder is one of the most common, disabling and persistent of the anxiety disorders. We have developed a cognitive therapy programme for adults, which specifically targets the maintaining factors outlined in Clark and Wells' (1995) model. Randomised controlled trials show that the treatment is highly effective. It is recommended as the first treatment option by NICE. However, there is room for further improvement. Key areas for research include: 1) adapting and evaluating the treatment for use with children and adolescents, 2) testing aspects of the cognitive model in children and adolescents, 3) understanding the mechanism of change, 4) developing an internet version of the treatment for fear of public speaking with associated experiments that characterise the cognitive processes distinguishing fear of public speaking from generalised social anxiety disorder. Students will be able to spend their day-a-week of clinical work in the Oxford Centre for Anxiety Disorders and Trauma supervised by Professors David M Clark, Anke Ehlers and colleagues. Other possible placements include research within a local IAPT service, or working with Christopher Fairburn's (eating disorders) or Daniel Freeman's (psychosis) clinical teams.

Philip Cowen

5-HT₄ receptor activation as a novel mechanism of antidepressant action

Abstract: Animal experimental studies have suggested that 5-HT₄ serotonin receptors may be important in mediating the antidepressant effects of SSRIs and targeting this receptor directly may work more quickly than conventional SSRI treatment. The study will involve a translational experimental medicine approach which employ models of emotional processing that can detect potential antidepressant effects of novel compounds in humans after only a few days of treatment. We will therefore use these models, which involve tasks of psychological performance and neuroimaging, to see whether a novel drug that selectively activates 5-HT₄ receptors can produce antidepressant-like changes in emotional processing in patients with depression.

We will carry out these studies in two separate groups of depressed patients: first, those who are not taking any antidepressant medication and second, people who have not experienced a good response to their current treatment. Positive results from one or both of these studies will lead on to formal clinical trials of a 5-HT₄ receptor agonist drug in depressed patients.

Reference

Duman RS. A silver bullet for the treatment of depression? *Neuron*. 2007; 55: 679-81.

Anke Ehlers

Overgeneralized fear responses in posttraumatic stress disorder

Abstract: Overgeneralization of conditioned fear responses is thought to contribute to the persistence of posttraumatic stress disorder. The empirical evidence for this hypothesis is relatively sparse. The project will explore a range of factors that may contribute to overgeneralised fear responses in this condition. A series of experimental studies with healthy volunteers and people who have experienced traumatic events will explore single trial associative learning, memory updating, and individual differences in perceptual and conceptual generalisation. Further

experiments will compare the effect of different interventions on overgeneralisation.

Russell Foster (joint with Daniel Freeman and Colin Espie, see below)

Elaine Fox

Cognitive Flexibility in Affective Disorders and Resilience

Abstract: Difficult to control repetitive negative thoughts are a transdiagnostic feature of affective disorders (anxiety and depression). Worry, for instance is one of the key cognitive characteristics of Generalized Anxiety Disorder (GAD) and rumination is a feature of depressive mood states. Cognitive models of anxiety and depression propose that worry/rumination is related to impaired executive functioning. The attentional control theory, for example, proposes that worry takes up limited attentional control capacity, making it more difficult to inhibit and shift attention away from negative intrusive thoughts. Translational research is essential in order to optimize future treatments for affective disorders. Our group is currently investigating the relation between worry and impaired working memory capacity (closely related to attentional control) in anxious individuals. However, there is some evidence that anxious and depressed individuals may also show reduced *cognitive flexibility*, or mental set shifting. Cognitive flexibility is a component of executive functioning and is often operationalized as task switching in a variety of cognitive tasks. For instance, if anxious/worrying individuals have difficulty in shifting their attention from negative thoughts, this may be reflected in reduced cognitive flexibility or cognitive inflexibility. Given a large literature showing that anxiety and depression are associated with biased cognition in terms of negative information, it will be especially interesting to examine cognitive flexibility in the context of emotional information. One aim of the proposed project is to investigate whether the presence of negative (and positive) information influences the relation between cognitive flexibility and worry/rumination. Using task-switching and other paradigms to measure cognitive flexibility in the context of emotional information, we aim to compare high-worriers and high ruminators to individuals who report that they do not worry or ruminate excessively. This work is important for an understanding of the cognitive aspects of the affective disorders and for the development of novel therapeutic interventions.

Relative to emotional vulnerability, far less is known about the cognitive characteristics of resilience and psychological wellbeing. Resilience is often described as the ability to react adaptively to changing situational demands. It is highly likely that cognitive flexibility might be one mechanism underlying such beneficial modulation of behavioural and emotional responses across changing situations. Since cognitive flexibility is important for emotion regulation, and effective emotion regulation in turn contributes to resilience, it has been proposed that cognitive flexibility in the context of emotional information may be essential for resilience. However, to date research on this possible relationship is relatively scarce. Therefore this project also has the option of investigating the relationship between cognitive flexibility in the context of emotional information and measures of resilience, psychological well-being, and emotion regulation, in healthy individuals.

Suggested Reading

Kashdan, T.B., & Rottenberg, J. (2010). Psychological flexibility as a fundamental aspect of health. *Clinical Psychology Review*, 30, 865-878. Doi: 10.1016/j.cpr.2010.03.001

Daniel Freeman, Colin Espie and Russell Foster

Sleep and persecutory delusions: theory and treatment

Abstract: This project will combine the important areas of sleep problems and psychotic experiences. A series of studies have begun to establish that disrupted sleep may be a causal factor in the occurrence and persistence of paranoia. This thesis will have three aims: to establish the causal connection between sleep and paranoia (e.g. carrying out a sleep restriction study); to develop the treatment of sleep disturbance in people with paranoia (e.g. to test out new techniques for stabilising sleep); and to test whether sleep can enhance the benefits of behavioural tests for paranoia. The person will be based in the Oxford Cognitive Approaches to Psychosis Unit at the University Department of Psychiatry (where there will be clinical experience) and the new Oxford Sleep and Circadian Neuroscience Institute (SCNi).

See: Freeman, D., Startup, H., Myers, E., Harvey, A., Geddes, J., Yu, L.-M., Zaiwalla, Z., Luengo-Fernandez, R., Foster, R., & Lister, R. (2013). The effects of using cognitive behavioural therapy to improve sleep for patients with delusions and hallucinations (the BEST study): study protocol. *Trials*, **14**, 214.

Colin A Espie, Simon Kyle & Ximena Onlin

Behavioural and neural changes in sleep-dependent cognition following therapeutic intervention for insomnia

Although restorative sleep represents a key factor for well-being and mental health, achieving it often poses a problem. Occasional sleep problems affect about one third of the adult population, while 10-12% of the population report persistent sleep disruption, severe enough to meet diagnostic criteria for clinical insomnia disorder [1]. The primary motivation to seek treatment is the impact of sleep disturbance on daytime functioning and quality of life, particularly cognitive performance, mood, and fatigue [2]. Sleep is important for memory as well as emotions, and changes in sleep-dependent cognition (e.g. impaired memory consolidation and altered emotion perception [3, 4]) have been reported in subjects suffering from poor sleep. In addition, these alterations in emotional processing might contribute to the maintenance of chronic insomnia due to heightened emotional reactivity and may explain why insomnia is a strong risk factor for the development of psychopathology [5, 6].

Although possible recovery of sleep-dependent cognition, as a result of successful insomnia treatment (e.g. cognitive behaviour therapy), could have implications for future therapeutic approaches, such a link has not yet been established. Nevertheless, as sleep and sleep-dependent cognition are so closely linked, a normalization of sleep might also have beneficial effects on memory and emotion regulation and, therefore, on daytime functioning with further implications for psychopathology. Crucial to the science of the field, however, is combined assessment of sleep-dependent cognition following insomnia treatment on a behavioural and neural level, in order to provide a more comprehensive understanding of therapeutic benefits relevant to daytime functioning.

Through this DPhil and related externally funded projects, we seek to enhance the understanding of insomnia related daytime impairments and their responsiveness to therapeutic intervention. In particular, we wish to a) evaluate and establish cognitive tasks sensitive to treatment related changes in sleep-dependent cognition; b) assess

changes in sleep-dependent cognition after successful insomnia treatment on a behavioural level; and c) investigate neural correlates of memory and emotion regulation.

The research will take place within the Sleep & Circadian Neuroscience Institute (SCNi) which is extensively funded by The Wellcome Trust, Sir Jules Thorne Charitable Trust, and the Sackler Foundation. There will be access to physiological monitoring equipment, neuroimaging and cognitive testing facilities and to engineering/digital health expertise, and a co-supervisor will be appointed to provide additional mentoring and support.

References:

1. Lichtstein, K.L., et al., *The epidemiology of sleep*. 2004, Mahwah, NJ: Lawrence Erlbaum Associates.
2. Morin, C.M. and R. Benca, *Chronic insomnia*. *The Lancet*, 2012. 379(9821): p. 1129-1141.
3. Beattie, L., et al., *Social interactions, emotion and sleep: A systematic review and research agenda*. *Sleep Med Rev*, 2014. 24C: p. 83-100.
4. Cipolli, C., M. Mazzetti, and G. Plazzi, *Sleep-dependent memory consolidation in patients with sleep disorders*. *Sleep Medicine Reviews*, 2013. 17(2): p. 91-103.
5. Harvey, A.G., *A cognitive model of insomnia*. *Behaviour Research and Therapy*, 2002. 40(8): p. 869-893.
6. Baglioni, C., et al., *Sleep and emotions: A focus on insomnia*. *Sleep Medicine Reviews*, 2010. 14(4): p. 227-238.

Supervisors:

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Dr Simon Kyle, Senior Research Fellow, SCNi, Nuffield Department of Clinical Neurosciences, <https://www.ndcn.ox.ac.uk/team/simon-kyle>

Dr Ximena Onlin, Post-Doctoral Researcher, SCNi, Nuffield Department of Clinical Neurosciences

Seena Fazel

Outcome measurement in forensic mental health

Improving outcome measurement is a national policy priority in mental healthcare. A recent 5-year plan proposed by NHS England's Mental Health Taskforce (Mental Health Taskforce, 2016) highlighted the need for more evidence on outcome measurement. This is important in forensic mental health where services that consume around one-fifth of the total mental health budget in England (Wilson, James, & Forrester, 2011) and for which outcomes remain poorly researched. Measurement of outcomes is necessary for the further development of effective services, provide more evidence for their potential impact on clinical care, and is increasingly used for planning recovery and treatment plans in a collaborative way with patients, carers, and commissioners (Joint Commissioning Panel for Mental Health, 2013).

A Health Technology Assessment review (Fitzpatrick, et al., 2010) of outcome measures used in forensic mental health research concluded that there was a paucity of research on outcome measures and identified a lack of consensus on the most relevant outcomes. The review suggested that outcomes should be considered according to four domains: clinical, rehabilitation, public safety, and quality of life. Currently, there is a focus on the public safety and clinical domains, and very little research on outcomes relevant to rehabilitation and quality of life.

The aims of the current project are:

- 1) To update the evidence base on outcomes in forensic mental health
- 2) To determine the most relevant measures
- 3) To operationalise these measures in a clinical tool
- 4) To pilot this tool in clinical services and evaluate its effectiveness

Methodology

A systematic review will be completed, which will update the Health Technology Assessment (HTA) review, taking into account new evidence since 2008 (when the search of the HTA review ended), and also survey those outcomes currently used in forensic mental health services. A modified Delphi process will be used to gain consensus on the most important and relevant outcomes measures identified in the four domains of clinical, risk, rehabilitation, and quality of life. This will include experts drawn from a range of disciplines and service users.

The chosen outcome measure will be operationalised using an adaptation of True Colours for forensic psychiatry that has already been piloted to investigate risk factors in this patient group (Gulati, et al., 2016). The aim is to develop a mobile app that allows clinicians and patients to jointly consider outcomes and track them over time. This will allow for therapies introduced at inpatient or outpatient level to be evaluated, particularly those working at a service level. It will also assist in the collection of data on a wider set of outcomes beyond clinical ones.

After development, the tool will be piloted in the clinical setting of a local forensic community service. This will look at the feasibility of its use in clinical practice and will compare it to the widely used Health of the Nation Outcome Score (HoNOS) Secure (Royal College of Psychiatrists, 2016). Determining which outcomes are most sensitive to change for particular interventions (e.g. to addition of a psychological or occupational therapy, or transfer between adult and forensic services), and how they can be interpreted will need to be examined, including investigating reliability, validity (compared to other outcome measures), and feasibility. This will provide observational evidence of changes in outcomes outside of clinical domains, which could form the basis of further research.

As part of this piloting, the researcher will have a clinical placement at the Oxford Clinic (low and medium secure unit in Littlemore, Oxford), which treats around 80 male and female inpatients at different levels of security, and from which 50-70 forensic psychiatry outpatients are also managed.

The main skills learnt will be systematic reviewing, Delphi method, and development and psychometric testing of new instruments.

References

- Fitzpatrick, R. et al., 2010. A systematic review of outcome measures used in forensic mental health research with consensus panel opinion. *Health Technology Assessment*, 14(18).
- Gulati, G. et al., 2016. Web-Based Violence Risk Monitoring Tool in Psychoses: Pilot Study in Community Forensic Patients. *Journal of Forensic Psychol Practice*, 16: 49-59.
- Joint Commissioning Panel for Mental Health, 2013. *Guidance for commissioners of forensic mental health services*.
- Mental Health Taskforce, 2016. *The five year forward view for mental health*.
- Royal College of Psychiatrists, 2016. *HoNOS Secure*. [Online] Available at: <http://www.rcpsych.ac.uk/crtu/healthofthenation/secure.aspx>.
- Wilson, S., James, D. & Forrester, A., 2011. The medium-secure project and criminal justice mental health. *Lancet*, 378: 110-111.

Seena Fazel & Belinda Lennox

Improving violence risk assessment in first episode psychosis

Absolute risks for interpersonal violence are high in severe mental illness. Within five years of diagnosis, one in 10 men with schizophrenia-spectrum disorders and one in 12 men with bipolar disorder are convicted of a violent crime. Rates increase to 39% for any interpersonal violence over 6-12 months in first-episode psychosis. Relative risks are also increased compared with the general population in more than 20 epidemiological studies.

To assess and reduce risks of interpersonal violence, many general psychiatric and almost all forensic psychiatric services routinely administer structured instruments to assist in risk stratification, and their use is recommended by clinical guidelines for schizophrenia in the US and UK. Stratification of risk assists in targeting resources, tailoring treatment and risk management, and informing decisions about more intensive service provision including hospitalization. Many tools are currently in use in psychiatry and criminal justice, but are limited by low to moderate accuracy, poor reporting standards, and inconsistent definitions of risk classifications. In individuals with psychosis, a 2011 systematic review identified that only 2 instruments have been validated, and in a total of 870 patients - since this review, 2 new instruments have been published. Another limitation of current approaches is that these tools consume resources by taking around 16 person-hours to complete, excluding the time taken for staff training. In contrast, other areas of medicine have developed scalable approaches such as the Framingham Risk Score or QRISK2 as an aid for clinical decision making. A key factor in their widespread use is their simplicity, external validity, and being linked to evidence-based interventions.

The Forensic Psychiatry Research Group have developed a web-based violence risk assessment for individuals with schizophrenia-spectrum disorders, which has been validated externally and with good measures of discrimination and calibration. It provides a probability score for violence in the next year, and categories all individuals with more than 5% as 'high' risk.

The current project will investigate how such a tool can be introduced and used in Early Intervention Services. Risk assessments are important for such services because forensic psychiatric services are restricted for those who have already committed serious offences, thus earlier evidence-based risk assessments can help determine resource allocation and potentially prevent a cycle of offending. The main components of the project will include:

1. Identifying the evidence base and theory for an intervention that reduces violence

risk in patients with psychosis, and then identify one that could be linked to risk assessment. This would involve a systematic review of the literature, and then developing an intervention that could be added to existing care for high risk individuals in discussion with clinical teams and patients.

2. Modelling how violence risk assessment could be incorporated into clinical practice including when it should be done, by what staff, and how the information could be used.
3. A feasibility study on completing a web-based risk assessment in a cohort of patients presenting to local Early Intervention Services, including examining barriers to implementation using qualitative methods.
4. Determining the best way to collect outcome information, information on intervention fidelity, possible mechanisms of treatment change, and relevant contextual factors that may explain variability.

The project will involve a clinical attachment at the local Early Intervention Services. The skills the candidate will learn include developing and evaluating complex interventions, systematic reviewing, and qualitative methods. It should assist in implementing a new evidence-based risk assessment into Early Intervention Services, and providing a framework with which to empirically test an intervention for patients at high risk.

John Geddes

Enhancing self management of bipolar disorder by relating patient reported measures of mood instability to underlying neural mechanisms in bipolar disorder

Abstract: Our current model of intensive self management of bipolar disorder relies on weekly or daily self ratings of mood. The aim of this project will be to produce a more informative short-term assessment of mood variability than currently provided by investigating and validating more intensive and objective measures of activity, sleep and neural activity as usable measures during the initial training phase of self-management training. The project will be based in the University Department of Psychiatry with weekly clinical activity and training provided in the specialist bipolar clinic directed by Prof Geddes. The project will use the innovative True Colours system for rating patient reported mood status and will sample from the existing OXTEXT cohort of intensively phenotyped and prospectively monitored patients with bipolar disorder. Self reported mood ratings will be correlated with (1) high frequency temporal instability of brain function assessed by MEG in the multimodal OHBA neuroimaging facilities and (2) remote monitoring of activity and sleep using the Proteus patch. Validated clinical measures will be integrated into the OXTEXT self-management programme and developed/piloted as a more efficient self management intervention.

Catherine Harmer

Using a neurocognitive model to understand antidepressant drug action

The mechanisms by which antidepressants improve the diverse range of symptoms seen in depression have remained elusive. However, recent evidence suggests that antidepressants can target key psychological processes important for the maintenance of illness, including so called negative bias. This involves over sampling and processing of negative information at the expense of more positive cues. Antidepressants can

reverse these negative biases very quickly in the treatment of depression (Harmer et al 2009) and are believed to lead to improved mood over time through interactions with the environment. The current project will involve testing whether these early changes in emotional processing (assessed with both behavioural and neuroimaging methods) can predict longer term treatment effects, as would be expected by this model. In particular, patients with depression will be randomised to receive a single dose of an antidepressant or placebo in a counterbalanced order before completing a battery of emotional processing measures. The ability of shifts in emotional processing bias with the drug treatment to predict clinical response after 6 weeks of treatment will also be assessed. This study will therefore contribute to our understanding of antidepressant drug action, using a cross-discipline approach, and have implications for the way in which we can detect and use information about early treatment response to improve treatment in depression. There will also be the opportunity to investigate specific neural mechanisms by which antidepressants affect the processing of emotional information which can be performed in healthy volunteers using MEG as well as fMRI.

Paul Harrison and Elizabeth Tunbridge

Calcium channels as therapeutic targets in psychiatry: using genomics to advance treatment

Recent genetic studies strongly implicate calcium signalling, especially that mediated by L-type voltage gated calcium channels (LTCC) in the aetiology of bipolar disorder. These genes are also involved in schizophrenia, sleep, and working memory. LTCC antagonists are already in use in cardiovascular medicine and have been used in bipolar disorder (based on earlier biochemical evidence for calcium abnormalities), but the existing drugs are not well suited for psychiatric indications, and our recent systematic review showed a lack of good evidence for efficacy (Cipriani et al, *Mol Psychiatry*, 2016 in press).

This DPhil project will help advance LTCCs as targets for psychiatric disorders, using a range of molecular and biochemical (and possibly bioinformatics) approaches applied to therapeutic developments, and will suit a psychiatrist interested in developing skills and knowledge in these areas. Prior experience in any of these concepts and methods would be desirable, but is not expected.

LTCC genes are expressed as a range of mRNA and protein variants (isoforms). There is preliminary evidence that these may differ between heart and brain, and vary across the lifespan, and differ in terms of their functional characteristics. Hence, a better understanding of the repertoire of LTCC isoforms is important for identifying which variant(s) will be more effective and selective for the brain, whilst avoiding cardiac side-effects. This project will investigate these issues in several ways:

- 1) The presence and relative abundance of brain LTCC mRNA isoforms will be determined using a combination of wet lab and possibly bioinformatics approaches. The cellular localisation of isoforms (i.e. to neurons or glia) will also be examined using in situ hybridization. There may be an opportunity to spend time working with our collaborators at the Genome Analysis Centre, Norwich, and/or the Lieber Institute for Brain Development (LIBD), Baltimore.
- 2) Similar methods will be applied to blood samples which are being collected in subjects participating in our clinical trial, OxCAMS. In OxCAMS, people with significant mood instability are randomised to the LTCC antagonist nifedipine, or placebo, for a two week period. They receive a multimodal and repeated battery of tests, amongst which are pre- and post-treatment blood samples, allowing us to assess whether treatment affects the expression of LTCC genes; this information may prove of value as a biomarker, and will also show whether nifedipine causes compensatory changes in expression of LTCCs.

- 3) Isoforms which are identified as being of particular interest from (1) will then be taken forward for functional screening. This will utilise transfected cell lines as well as examination of induced pluripotent stem cells which have been created from patients with bipolar disorder. Possible readouts include electrophysiological, biochemical, and molecular parameters. The extent to which the candidate works on (3) will depend on their interests, the progress of 1) and 2), and other developments in the field in the interim.

The work will be based in the Neurosciences Building, University Department of Psychiatry, at the Warneford Hospital. Up to a day a week will be spent participating in our research clinic, in the NIHR Oxford cognitive health Clinical Research Facility, wherein a range of innovative approaches to diagnosis, assessment, and treatment of mood disorders and mood instability are used. Other clinical placements are also possible.

The project benefits from related ongoing work which is being carried out as part of a Wellcome Trust Strategic Award, and from collaborations with the Structural Genomics Consortium, The Genome Analysis Centre, and the LIBD mentioned above.

Applicants are invited to contact either supervisor for further information and informal discussions. elizabeth.tunbridge@psych.ox.ac.uk or paul.harrison@psych.ox.ac.uk

Paul Harrison

Do calcium channel antagonists stabilise mood? A genetically informed, placebo controlled, double blind, randomised experimental medicine study

Calcium signalling is central to current theories of bipolar disorder, for two main reasons. First, cellular calcium signalling is altered in people with the disorder. Second, recent data show that L-type calcium channel genes, especially *CACNA1C* (which encodes the $Ca_v1.2$ subunit), contribute to the genetic aetiology. L-type calcium channel antagonists are widely used to treat hypertension, and uncontrolled data suggest they may have some efficacy for the treatment of mania. However, there are no good studies showing whether these drugs stabilise mood, and none which have investigated their effect on brain function.

Forty subjects with high mood instability, and who have the *CACNA1C* bipolar risk genotype, will be recruited. After a 3 week assessment period (which will include remote monitoring of mood and activity, cognitive tasks delivered via an app, MEG and fMRI scans, and a range of biochemical investigations), they will be randomised to receive nifedipine (a licensed calcium channel antagonist) or matched placebo for a further 3 weeks. They will continue to be monitored closely during this time, and repeat neuroimaging and biochemical measurements taken. Both longitudinal and cross-sectional comparisons will be made.

The study will show whether and how calcium channel antagonists stabilise mood and, if positive, will provide a rationale and basis for large scale clinical trials in patients with bipolar disorder. The study also serves as an exemplar of how experimental medicine approaches can be applied to study of psychiatric disorders and their treatment.

The candidate will gain training in: psychological and cognitive assessments; multimodal functional brain imaging; design and execution of randomised clinical trials; genotyping; calcium biology; and bipolar disorder itself.

This project will be part of a large multidisciplinary study of mood instability and bipolar disorder called CONBRIO (<http://conbrio.psych.ox.ac.uk/home>), funded by a

Wellcome Trust Strategic Award. It will be based in the specialist bipolar disorder research clinic situated in the Clinical Research Facility at the Warneford Hospital. Research assistants and research nurses will assist with the day-to-day running of the trial.

Potential applicants are welcome to contact paul.harrison@psych.ox.ac.uk for further information and informal discussion.

Masud Husain

Motivation and decision-making in brain disorders

Abstract: Deficits of motivation and decision-making, e.g. apathy and impulsivity, are common clinical problems associated with many different kinds of brain disorder. They have a profound impact on the lives of people but currently there is little in the way of treatment for these complex conditions.

We're interested in understanding mechanisms that underpin such altered behaviours and developing programmes to treat them. Our experimental methods have been developed from basic cognitive neuroscience for application to patient groups.

We use behavioural techniques to assess sensitivity to rewards and the effort required to acquire them, as well as the ability to use feedback to learn from previous poor decision-making. We use structural and functional imaging to relate functional disturbances to alterations in brain networks.

We study patients with stroke, Parkinson's disease and Alzheimer's disease. Our intervention techniques include drug treatments and computerised training programmes to adaptively modulate behaviour.

If you're interested to learn more visit www.masudhusain.org.

Heidi Johansen-Berg

Impact of sleep quality on rehabilitation outcomes following stroke

Rehabilitation after stroke depends on processes of brain plasticity and learning. It is well established that sleep is critical for consolidation of certain types of learning, such as learning of new motor skills. There is some evidence that sleep quality is poor in older people in general, and in stroke sufferers and people in in-patient settings in particular. Therefore, improving poor sleep, and therefore maximising consolidation of new memories, is a potential 'back door' route to improving rehabilitation outcomes after stroke.

However, there is remarkably little research on the prevalence of sleep disturbance in individuals after stroke. It is unclear whether sleep problems are a risk factor or consequence of stroke. It is unknown whether sleep disturbance contributes to rehabilitation outcomes and whether interventions to improve sleep quality could enhance outcomes.

The proposed project would involve sleep quality assessments (using accelerometry, EEG, and questionnaires) in patients after stroke, in both home and in-patient settings.

Sleep measures would be related to impairments and to rehabilitation outcomes. Interventions (e.g., sleep therapy, melatonin) would be trialled.

The project would involve clinical placements in year 1 under the supervision of Dr Udo Kischka (Oxford Centre for Enablement).

Belinda Lennox and Camilla Buckley

Optimising treatment for psychosis and autoimmune encephalopathy

Joint supervisors: Dr Belinda Lennox (psychiatry) and Dr Camilla Buckley (NDCN)

We run a joint neuro-immunological and psychiatric clinical service for autoimmune encephalopathy with regional and national referrals. The proposed project will be based alongside this clinical service.

We have found that alongside the classical syndrome of encephalitis (involving seizures, cognitive impairment, movement disorder and autonomic disturbance), a proportion (6.5%) of patients with a primary psychotic illness, without other features of encephalitis also have antibodies against neuronal cell surface targets (including NMDAR, VGKC).

The project will involve characterising the clinical and neurocognitive phenotype of this new disorder, and the response to treatment with both psychiatric and immunological medications.

Charles Newton

Autism in children of immigrant parents

Immigration is recognised as a risk factor for the development of autism in the children born to mothers from Africa and Caribbean in particular. It is not clear the mechanisms of this risk. Possible explanations include: genetic susceptibility, higher incidence of brain insults, men seeking immigrant partners who are less aware of autism related social problems, difficulty in finding a partner with increased paternal age, selection bias of immigrants and low levels of Vitamin D in immigrant mothers. We want to examine the mechanisms that lead to increased risk of autism in children born to immigrant mothers.

Kia Nobre

Neural dynamics of regulatory mechanisms in cognition

Abstract: Our perception and cognition are shaped by numerous modulatory signals, related to our task goals, expectations, memories, motivation, and emotions. We are interested in understanding the neural mechanisms and dynamics of these various sources of biases, and in understanding how they are compromised during ageing and in neurodegenerative and neuropsychiatric disorders. Studies would be available looking at the integrity and dynamics of networks of brain regions derived from magnetoencephalography (MEG) data recorded at rest and during cognitive tasks. We are also involved in the Collaborative Network for Bipolar Research to Improve Outcomes (conBRIO, <http://conbrio.psych.ox.ac.uk/home>). Specifically, we are studying the influence of mood and mood instability on cognition using daily behavioural testing as well as its neural basis using MEG and structural and functional MRI.

For more information on specific projects and methods, please refer to the web sites of the Oxford Centre for Human Brain Activity (OHBA, <http://www.ohba.ox.ac.uk>) and the Brain & Cognition Lab (<http://www.brainandcognition.org>).

Michael Sharpe and Jane Walker

Psychological and psychiatric studies in the medically ill

Abstract:

Clinical Unit: Psychological Medicine (psychiatry and psychology service) and relevant medical settings in the Oxford University Hospitals NHS Foundation Trust.

You will work with Professor Sharpe, Dr Walker and other members of the Psychological Medicine Research (PMR) team and also with members of the award winning linked clinical service.

Projects available (to be agreed in discussion prior to application) include:

- (a) Secondary analysis of large descriptive and trial datasets of psychiatric illness in patients with cancer.
- (b) Descriptive and intervention studies of very high users of general medical care who have psychiatric illness.
- (c) A clinical trial of proactive psychiatric care for elderly patients admitted to acute hospitals.
- (d) Evaluation of a system for care for patients with depression at the end of life.

Research methods taught include:

Qualitative and quantitative descriptive methods, secondary analysis of large datasets, complex intervention design and clinical trial methods.

You will also gain experience of working as a member of a multidisciplinary clinical research team whilst leading on an aspect of the work and writing this up for a DPhil.

[Access to clinical services agreed.]

Alan Stein

The Influence of Perinatal Psychological Disorders on Child Development

Abstract: Our main interest concerns the influence of perinatal depression and anxiety on parent---infant interaction and child development. We investigate the mechanisms underlying the relationship between parental disorders and child development and use this to develop targeted interventions.

The studentship will enable investigation of the pathway from parental disorder to child outcome. Of particular interest is the way in which disturbances in cognitions (including rumination and worry) can affect parenting capacities and how these different parenting capacities may in turn impact on child outcomes. The student could investigate aspects the three parenting capacities that have been hypothesised to mediate the effects on child cognitive and emotional development and behaviour:

- 1) Parental focus of attention to child's facial and vocal communications and the associated contingent appropriate responsiveness and
- 2) Parental emotion scaffolding (principally comprising warmth, support and low

levels of intrusiveness), particularly during potentially stressful situations to support infants to develop their own emotional regulation

3) Parental capacity to treat a child as a psychological agent (i.e. as someone with feelings and intentions).

Studies can include observational work, experimental studies or a brief intervention.